Acute effects of repetitive peripheral magnetic stimulation following low-intensity isometric exercise on muscle swelling for selective muscle in healthy young men

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Abstract

Repetitive peripheral magnetic stimulation (rPMS) is a non-invasive stimulator that can induce strong muscle contraction in selective regions. This study aimed to measure acute changes in skeletal muscle thickness induced by rPMS following a low-intensity exercise. Fifteen healthy young men performed an isometric knee extensor exercise at 30% of maximum strength consisting of three sets of 10 contractions on their dominant leg. rPMS was then applied on the vastus lateralis (VL) at the maximum intensity of the rPMS device. Muscle thicknesses of the rectus femoris (RF) and VL were measured using an ultrasound device and were compared among baseline, post-exercise, and post-rPMS. There were significant increases in muscle thickness of both the RF and VL post-exercise compared with baseline values (RF: baseline; 24.7±2.4, post-exercise; 25.3±2.4 mm, $p = 0.034$, VL: baseline; 27.0±2.8, post-exercise; 27.4±2.8 mm, $p = 0.006$). Compared with post-exercise, there was a significant increase post-rPMS in only the VL (VL: post-rPMS; 28.3±2.9 mm, $p = 0.002$). These findings suggest that low-intensity isometric exercise can induce acute increases in muscle thickness (muscle swelling) in synergist muscles, and rPMS following exercise can induce further acute muscle swelling via repetitive muscle contraction.

Keywords

non-invasive peripheral stimulation; knee extensor; low-intensity exercise; acute muscle swelling; peripheral magnetic stimulation

Introduction

Non-invasive peripheral stimulation is a method used to contract the muscle by applying an external stimulating device over a nerve, muscle, or spinal root to depolarize the conductive structures in the peripheral nervous system. Non-invasive peripheral stimulation such as neuromuscular electrical stimulation or repetitive peripheral magnetic stimulation (rPMS) is used in research and clinical settings (Beaulieu & Schneider, 2015; Hasegawa et al., 2011; Nardone et al., 2015). Although transcutaneous electrical nerve stimulation causes skin pain due to an unavoidable stimulation of skin nociceptors, rPMS can induce muscle contraction without pain. Electromagnetic fields induced by rPMS produce eddy currents in the peripheral neuromuscular system that bypass cutaneous pain receptors (Barker, 1991). This characteristic of rPMS enables the stimulation of muscle contractions with less pain; therefore, rPMS can induce a stronger torque compared to electrical stimulation when stimulated at an intensity the participant can tolerate (Han, Shin, & Kim, 2006).

Some studies reported the effects of rPMS on the increase in excitability of the primary motor cortex and improvement of motor functions in stroke patients (Beaulieu, Masse-Alarie, Camire-Bernier, Ribot-Ciscar, & Schneider, 2017; Sakai, Yasufuku, Kamo, Ota, & Momosaki, 2019). Selective rPMS of the multifidus muscles in participants with low back pain improved excitability of the primary motor cortex and activity of the muscle during movement (Masse-Alarie, Beaulieu, Preuss, & Schneider, 2017). Similar to these findings, previous studies investigating the effects of rPMS reported excitability of the nervous system or improvement of motor functions as the main outcome measure. rPMS is thought to improve sensorimotor functions by modifying the central nervous system via the ascending pathway (Kumru et al., 2017). For this reason, rPMS is often used in studies focused on the improvement of neurological functions in stroke patients (Beaulieu & Schneider, 2013; Momosaki, Yamada, Ota, & Abo, 2017; Sakai et al., 2019). The ability for rPMS, to induces a painless muscle contraction (Han et al., 2006) makes it possible to promote greater-intensity muscle contractions without pain and induce repetitive contractions that can cause muscular morphological changes such as acute muscle swelling. A previous study based on *in vivo* mouse muscle injury models showed that magnetic stimulation caused myofiber hypertrophy (Stolting et al., 2016). Nevertheless, to the best of our knowledge, only one study has investigated the effects of rPMS on muscle morphology in humans. The study showed that rPMS could improve muscle strength after a 5-week intervention but not induce muscle hypertrophy (Yang, Jee, Hwang, & Sohn, 2017). The application of rPMS alone might not produce a sufficient trigger to change the muscle morphology.

High-intensity training is recommended (American College of Sports Medicine, 2009); however, in older individuals or patients with cardiorespiratory or orthopedic problems, attention needs to be paid to the safety of high-intensity training. High-intensity training cannot be applied to all patients. In contrast, low-intensity training is widely used in clinical settings and rehabilitation because it can be carried out with low risks of increasing blood pressure or joint stress. A combination of non-invasive external stimulation and normal low-intensity exercise may be a potential effective method. For example, a previous study showed that the combination of whole-body neuromuscular electrical stimulation and voluntary exercise induced greater metabolic responses than exercise alone (Watanabe, Yoshida, Ishikawa, Kawade, & Moritani, 2019), suggesting that the combination could enhance the metabolic response to the same level as a high-intensity exercise. However, the coil used in the rPMS device gets overheated after repeated use, limiting the number of stimulation repetitions. Although rPMS alone may not be sufficient in stimulating a muscle anabolic response (Yang et al., 2017), the combination of rPMS and low-intensity exercise may induce metabolic responses.

Acute changes in skeletal muscle include swelling that is associated with hypertrophy

(Schoenfeld, 2013). Muscle swelling occurs as a result of increasing phosphocreatine and hydrogen ion accumulation because of blood lactate elevations (Gonzalez et al., 2015), leading to a state of increased muscle cross-sectional area or muscle thickness because of an increased extracellular fluid (Taniguchi, Yamada, & Ichihashi, 2020). A recent study suggested that muscle swelling assessed by increased muscle thickness immediately after exercise using ultrasonography was related to subsequent muscle hypertrophy (Hirono et al., 2020).

Because coil overheating limits the use of the rPMS device, the combination of exercise and rPMS may be applied in clinical situations. The rPMS device does not require skin treatments and can be placed over the clothes; therefore, this device can be used easily and immediately following exercise. The present study aimed to investigate the effect of rPMS combined with low-intensity exercise on acute muscle swelling. Thus, we compared muscle swelling immediately after a low-intensity knee extension exercise with muscle swelling immediately after selective rPMS following exercise. We hypothesized that muscle swelling in the knee extensor muscles would occur immediately after a low-intensity knee extension exercise, while further muscle swelling in a selective stimulated region would occur after rPMS. These examinations may be useful in suggesting a new exercise method that reduces the amount of a patient's voluntary muscle activity but still have effects on selective muscles.

Materials and Methods

Participants

Fifteen healthy young men participated in the present study (age, 25.5 ± 3.7 years; body weight, 62.9 ± 6.2 kg; height, 171.1 ± 7.1 cm). None of the participants had a history of musculoskeletal and neurological problems in their legs. The study was approved by the investigators' institutional ethics committee (R1918) and conformed to the principles of the Declaration of Helsinki. Before participating in the study, the participants received a detailed explanation of the protocol and gave written informed consent.

According to our preliminary data (n = 5) that investigated the acute increase of muscle thickness in VL after exercise and rPMS, power analysis for paired t-tests using an effect size of 0.870, with an α-error of 0.05, and a power of 0.80 revealed that the required sample size was 13 participants (G*Power 3.1, Dusseldorf, Germany). Therefore, a total of 15 participants volunteered and were recruited in this study.

Procedure

The experimental procedure followed for the present study is detailed in Fig. 1. Measurements, exercises, and applications of rPMS were performed on the participants' dominant legs, determined by which leg they would use to kick a ball. First, muscle thickness was measured using an ultrasound device in the supine and rest positions (Pre). Then, maximum isometric knee extension strength was measured in the sitting position. After a rest interval of more than 2 min, the participants performed low-intensity knee extension exercises. Immediately after the exercise, muscle thickness was measured again in the supine position (Post 1). After the second measurement of muscle thickness, rPMS was applied on their lateral thigh over the vastus lateralis (VL) in the sitting position (Fig. 2). Immediately after the application of rPMS, muscle thickness was measured in the supine position (Post 2).

Measurements for muscle thickness

The participants were instructed to lie in the supine position and relax. Muscle thickness of the rectus femoris (RF) and VL were measured on B-mode images in the transverse plane taken using a wireless ultrasound device with a 10-MHz linear array probe in MSK preset (SONON 300L; Healcerion Co., Ltd, Seoul, Korea). B-mode images of the RF were obtained at the median of the distance from the anterior superior iliac spine to the superior border of the patella. B-mode images of the VL were obtained at the median of the distance from the greater trochanter to the lateral condyle of the femur. These points were marked with a semipermanent ink so that the measurements could be performed at the same locations. B-mode images were obtained in minimal contact force when the femur was clearly seen (Pigula-Tresansky et al., 2018), and a sufficient amount of water-soluble gel was applied to the skin. Muscle thickness was determined as the distance between the superficial and deep aponeuroses. Thickness of each muscle was measured three times, and the averaged value was used in subsequent analyses.

To confirm the reliability of the measurements, muscle thicknesses of the RF and VL in the dominant leg were measured three times. The intraclass correlation coefficient (1, 3) of the three measurements of muscle thickness of the RF and VL were 0.997 and 0.994, respectively. In addition, the coefficient of variation (CV) and the standard error of the mean (SEM) among the three measurements in each participant were calculated. The mean ± standard deviation of CV of the RF and VL were 0.7 ± 0.4 % and 1.1 ± 0.6 %, respectively. The mean ± standard deviation of SEM of the RF and VL were 0.11 ± 0.05 mm and 0.17 ± 0.09 mm, respectively.

Maximum isometric strength and low-intensity exercise

Maximum isometric torque was measured, and low-intensity exercise was performed using the isometric mode of a dynamometer (Biodex system 4; Biodex Medical Systems, Inc., Shirley, New York, USA). The participants were seated on the dynamometer chair, and their trunk and pelvis were fixed with inelastic belts with their hip joints at 80° flexion (0° corresponds to neutral position between the trunk and the thigh). The lateral epicondyle of the femur was aligned to the dynamometer's axis of rotation, and the shank of the dominant leg was fastened to the lever arm. They gripped the levers on both sides of the chair. The knee flexion angle was set at 90° while measuring the maximum isometric knee extension strength and performing the low-intensity isometric exercise (0° corresponds to full extension).

Maximum isometric knee extension torque was measured before exercise. After sufficient warm-up, the participants exerted their maximum voluntary knee extension torque for approximately 3 s with verbal encouragements. The peak torque during a 3-s contraction was defined as maximum strength. The measurements were performed twice with an interval of 60 s, and the largest value was defined as the maximal voluntary contraction (MVC). After more than 2 min of rest, the participants were asked to report their self-perceived fatigue in their knee extensors. After the investigator confirmed they were not fatigued, the participants performed the isometric knee extension exercise at the target torque of 30% of MVC. The low-intensity protocol exercise is widely used in clinical settings and rehabilitation. Exerted torque and the target torque were displayed on a monitor that was located 1 m in front of the participants. They were instructed to exert their knee extension torque over the target torque of 30% of MVC during their voluntary contractions. The low-intensity isometric exercise was performed in three sets; one set comprised 10 repetitions of 5 s contractions and 5 s rest intervals, and inter-set intervals were 60 s. Each exerted torque during the low-intensity exercise was recorded, excluding the initial 1-s torque, which was considered the increasing phase. The recorded torques were normalized to MVC, and the averaged torque (%MVC) was calculated.

Repetitive peripheral magnetic stimulation

rPMS was delivered over the participants' lateral thighs on the dominant leg. The participants sat on the dynamometer chair with 90° knee flexion, which was the same position as the exercise task. rPMS was applied for two sessions using the round coil of the rPMS device (Pathleader; IFG Co., Sendai, Japan) at a frequency of 50 Hz: one session consisted of 50 contractions with a stimulation duration of 1 s and an inter-stimulation interval of 3 s; the inter-session interval was set at 100 s. The total number of stimuli were 5,000 pulses. Immediately before rPMS sessions, test stimulations were applied at about 5–6 contractions with incremental intensity to familiarize rPMS (from Levels 50 to 100). The maximum intensity of the device, level 100, indicates approximately 0.9 Tesla. Since the study aimed to induce muscle swelling by muscle contractions, rPMS was applied to all participants at the maximum stimulation intensity level of the device (Level 100), and all sessions were completed without stopping because of overheating. No participant in this study halted the stimulation due to pain or an uncomfortable feeling during the rPMS. Compared with other studies targeted at sensorimotor impairments (Beaulieu & Schneider, 2015), the intensity was greater, and the protocol might be efficient in physiological benefits. The peak torque in each contraction of all twitch torques induced by rPMS was recorded using the dynamometer, and the average and standard deviation of all 100 contractions were calculated.

Statistical analyses

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS version 22.0; IBM Japan, Inc., Tokyo, Japan). Shapiro-Wilk test was performed to test for normality of muscle thickness data. Analyses of variance (ANOVA) or Friedman test was performed within factors of time (Pre, Post 1, Post 2) for each muscle (RF and VL) to analyze the main effects of the changes in muscle thickness. When a main effect was identified as statistically significant, paired t-tests or Wilcoxon signed-rank tests with Bonferroni corrections were used. Effect sizes (ESs) were calculated between Pre and Post 1, between Pre and Post 2, and between Post 1 and Post 2 using Cohen's d. The statistical significance was set at $p < 0.05$.

Results

Changes in muscle thickness

The Shapiro-Wilk tests indicated that the thickness of the VL at Post 1 and Post 2 and the RF at Post 2 were not normally distributed ($p < 0.05$). Therefore, the Friedman tests were conducted to analyze the variables. The changes in muscle thickness of the RF and VL are shown in Fig. 3. The Friedman tests revealed significant main effects for the VL ($p < 0.001$) and RF ($p < 0.001$). The Wilcoxon signed-rank tests with Bonferroni corrections revealed that the VL at Post 1 was significantly greater than that at Pre (Pre, 27.0 ± 2.8 mm; Post 1, 27.4 ± 2.8 mm; ES = 0.15, p = 0.006), and the VL at Post 2 was significantly greater than that at Pre (Post 2, 28.3 ± 2.9 mm; ES = 0.44, p = 0.001) and Post 1 (ES = 0.29, p = 0.002). Post-hoc analysis showed that the RF at Post 1 was significantly greater than that at Pre (Pre, 24.7 ± 2.4; Post 1, 25.3 ± 2.4 mm; ES = 0.22, p = 0.034), while the RF at Post 2 was significantly lower than that at Post 1 (Post 2, 24.8 ± 2.4 mm; ES = 0.21, p = 0.007). There was no significant difference in the muscle thickness of the RF between Pre and Post 2 (ES = 0.01, p = 1.0).

Exerted torques during low-intensity isometric exercise and rPMS

The average torque during the low-intensity isometric exercise was 30.2 ± 2.4 % MVC. The average twitch torque of all 100 contractions induced by rPMS was 8.8 ± 3.3 % MVC (absolute torque value: 16.2 ± 4.6 Nm).

Discussion

We investigated muscle swelling after a low-intensity isometric knee extension exercise and additional muscle swelling after applying rPMS on the VL following exercise in healthy young men. In agreement with our hypotheses, muscle swelling of both the RF and VL occurred after the low-intensity exercise, and further muscle swelling after rPMS was only observed in the VL. This is the first study showing that the combination of rPMS and a low-intensity exercise induces further muscle swelling.

Although muscle swelling of both the RF and VL occurred after the low-intensity exercise, the ESs were small (ES = 0.22 and 0.15, respectively). The sensitivity of measuring ultrasound images of RF and VL assessments performed at only one site rather than multiple sites could have led to the small ESs. After the rPMS following exercise, further muscle swelling of the VL occurred due to selective stimulation (ES = 0.44). The change in muscle thickness after the low-intensity exercise in the present study was smaller than the change after a high-intensity exercise in a previous study (Vieira et al., 2018). However, muscle hypertrophy occurred when an exercise with acute changes in the small ES was performed (Fahs et al., 2015). A previous study that applied a total of 1,500 pulses per session recorded no muscle hypertrophy after the rPMS intervention (Yang et al., 2017). The present study applied rPMS at its maximal intensity on the device (0.9 Tesla), and the number of pulses were greater (5,000 pulses) than the previous study. Future researches should clarify the intensity, the number of pulses, and the strength of the evoked torque required for morphological changes.

We used the rPMS device with a round coil that enabled stimulation of deeper and larger areas than with a figure-of-8 coil (Nicola Smania et al., 2003; N. Smania et al., 2005). Considering the result that muscle thickness of the RF at Post 2 returned to baseline, rPMS may stimulate only the VL selectively without inducing contractions of the surrounding muscles. Another result of the present study revealed that averaged twitch torques of all 100 contractions induced by rPMS with maximum intensity were about 9% of MVC. The increase in VL muscle thickness following voluntary exercises at 30% of MVC had a small ES (ES = 0.15), whereas the increase in VL muscle thickness following rPMS at only 9% of MVC was larger (ES = 0.29). Even if the deep muscle could contract due to the eddy currents, the evoked torque from the deep muscle was probably weak because the strength of the generated magnetic field was inversely proportional to the square of the distance. At the time of the rPMS application, the lateral part of the muscles (VL and perhaps vastus intermedius under the VL) produced 9% torque of the whole knee extensor muscle capacity. Therefore, it was presumed that great and repeated muscle contractions were induced at the stimulated site. After wards, metabolic mechanisms would be stimulated, and intra- and extracellular water balance in the muscle would be altered due to increases in phosphocreatine and hydrogen ion accumulation, resulting in muscle swelling (Allen, Lamb, & Westerblad, 2008; Taniguchi et al., 2020; Watson, Garner, & Ward, 1993). Although we assessed muscle swelling in only one site of the VL, it will be interesting to assess muscle swelling in distal or proximal non-stimulated sites. The effect of rPMS on muscle tension in the whole muscle should be evaluated with an intervention with larger sample sizes in future studies. In addition, the mechanism of motor unit or muscle fiber recruitment by the rPMS remains unclear. Although a previous study on *in vivo* injured muscle of mice reported that the magnetic stimulation caused muscle regeneration and induced type I myofiber hypertrophy (Stolting et al., 2016), the characteristics of rPMS for recruitment of motor units or muscle fibers *in vivo* remains unclear. The recruitment pattern of motor units induced by rPMS in human is interesting for investigating in future.

The characteristic of stimulating selective vastus muscles of the quadriceps femoris muscles may be expected to be applied in various clinical situations. Patients with knee osteoarthritis have been reported to have less muscle mass of the vastus muscles compared with healthy individuals (Aily et al., 2019; Taniguchi et al., 2015). In knee extension exercises, it is generally not possible to contract only one of the synergist muscles to enable contraction of only the VL; rather all synergist muscles contract. Considering that individual differences in force distribution among synergist muscles occur while exerting muscle force (Crouzier et al., 2020; Hug et al., 2015; Hug et al., 2019), general strength training may not improve the muscle mass of the vastus muscles in patients with less force exertion. Applying rPMS selectively to atrophied muscle may improve imbalance among synergist muscles. In addition, because imbalance of muscle forces among hip muscles could increase joint stress (Lewis, Sahrmann, & Moran, 2007), it is expected that there will be clinical applications in the prevention of muscle atrophy and promotion of muscle hypertrophy for selective muscles in various joints. The effects of selective stimulation of various muscles on kinesiology or motor functions should be investigated in future studies.

This study had some limitations. We recruited healthy young men; therefore, the clinical application in older individuals or patient needs to be considered carefully. Specifically, applying magnetic stimulation to an area around artificial joints or fixations of metallic materials is difficult. Future studies should investigate the effect on the promotion of muscle hypertrophy and the prevention of muscle atrophy in patients. Another limitation was that we examined only acute changes after exercise. Therefore, it is unclear whether applications of rPMS do, in fact, induce chronic muscle hypertrophy. It would be interesting to determine whether the continuous application of rPMS changes muscle morphology and improves muscle strength or motor performance. Further investigations are expected in the future. Additionally, a methodological limitation on the measurements of muscle thickness should be discussed. We assessed only one site each of the RF and VL and measured only one distance between the superficial and deep aponeuroses. Although the reliabilities high, assessment at one location could lead to mis-interpretation of measurements because muscle morphology is non-uniform (Wakahara, Fukutani, Kawakami, & Yanai, 2013). Future studies should focus on whole muscle changes. Finally, the negative aspects of peripheral magnetic stimulation should be considered. When applying the stimulation in patients or older adults, it cannot be denied that non-voluntary stimulated muscle contractions can lead to an unaccustomed activation pattern among synergists, which can in turn lead to an unaccustomed stress or strain within the tissue, leading to muscle damage. Considering other aspects, the magnetic stimulator is expensive, repetitive use leads to be overheating it, and it cannot be used on metallic objects such as artificial joint sites. These aspects should be considered in future study and clinical settings.

In summary, we demonstrated that low-intensity exercises increased muscle thickness at one site of RF and VL. Applying rPMS following exercise induced further increased muscle thickness of the VL which was selectively stimulated. Further clinical applications of rPMS in the prevention of muscle atrophy, promotion of muscle hypertrophy, and improvement of muscle imbalance are expected in the future.

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Disclosure statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Figure legends

Figure. 1

Experimental procedure

Figure. 2

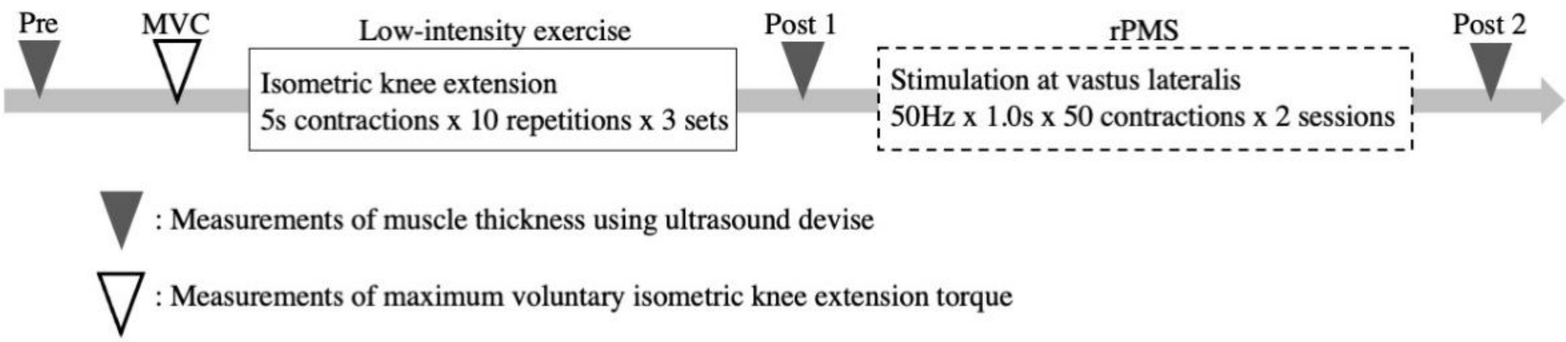
Applying the coil of the rPMS device over the VL

rPMS, repetitive peripheral magnetic stimulation; VL, vastus lateralis

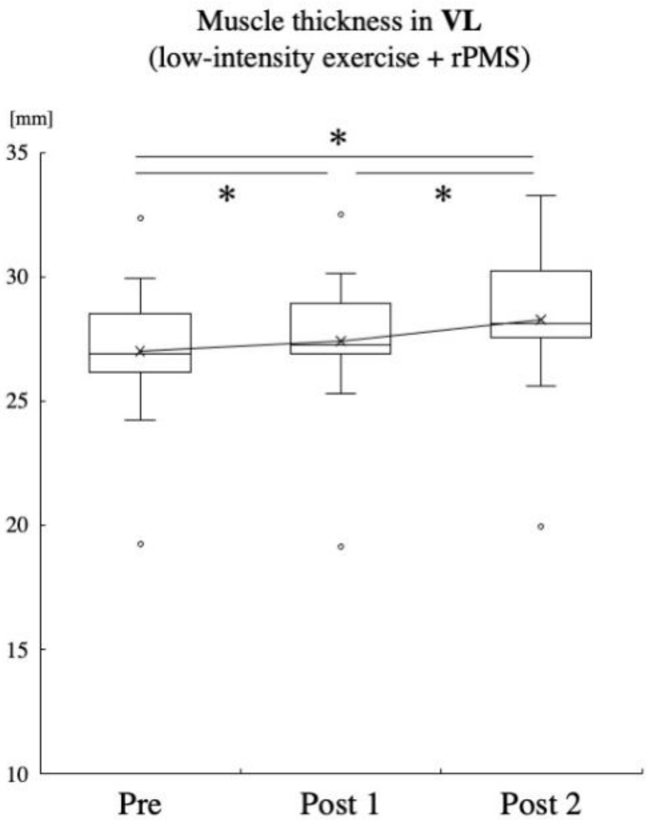
Figure. 3

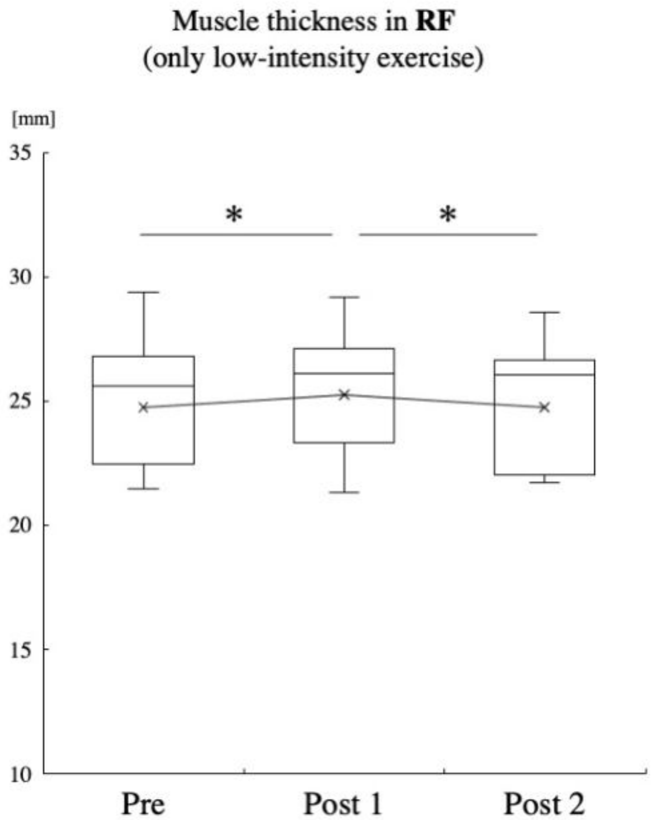
Changes in muscle thickness before and after a low-intensity exercise and rPMS

The left box plots represent muscle thickness of the VL. The right box plots represent muscle thickness of the RF. Compared with muscle thickness before exercise (Pre), muscle thickness of the VL and RF increased after the low-intensity exercise (Post 1). After rPMS of the VL (Post 2), muscle thickness of the VL increased significantly compared with Post 1, and muscle thickness of the RF decreased significantly. * represents significant difference ($p < 0.05$). The horizontal line in the box represents the median value. The upper and lower hinges correspond to the first and third quartiles. The whiskers extend from the hinge to the maximum or minimum value within ±1.5 × inter-quartile range of the hinge. Individual data points are values outside these ranges. An X marker represents the mean value. rPMS, repetitive peripheral magnetic stimulation; VL, vastus lateralis; RF, recurs femoris


Pre
MVC
Low-intensity exercise
Isometric knee extension
5s contractions x 10 repetitions x 3 sets
Post 1
rPMS
Stimulation at vastus lateralis
50Hz x 1.0s x 50 contractions x 2 sessions
Post 2
: Measurements of muscle thickness using ultrasound devise
: Measurements of maximum voluntary isometric knee extension torque


Pathleader
COMFORT STOP


Muscle thickness in VL
(low-intensity exercise + rPMS)
[mm]
35
30
25
20
15
10
*
*
*
Pre
Post 1
Post 2


Muscle thickness in RF
(only low-intensity exercise)
[mm]
35
30
25
20
15
10
*
*
Pre
Post 1
Post 2